REMARKS

Claims 20, 25, 66-70 and 72-76 presently appear in this case. No claims have been allowed. Claims 21, 22, 25, 68, 71, and 72 have been withdrawn from consideration. The official action of April 11, 2007, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to the use of NIK and related molecules for binding to cγc and inhibiting cγc/NIK interaction, thus modulating signal activities controlled by cytokines and NIK induced NF-κB activation.

Claims 21, 22, 25, 68, 71 and 72 have been withdrawn from further consideration as drawn to non-elected inventions, there being no allowable generic or linking claim. These claims are nevertheless being allowed to remain in the case pending the allowability of generic and/or linking claims. It should be noted, however, that the examiner is incorrect in stating that rheumatoid arthritis is a disease involving IL-2; rather, it is a disease involving NF-κB activation.

The examiner states that the declaration of May 17, 2005, is objected to for failing to recite priority to Israel 149217 or Israel 152183. However, the examiner's attention is invited to 37 CFR 1.63(c)(2), which states that unless the information is supplied on an application data sheet (ADS) the declaration must identify foreign priorities. An ADS was filed upon the filing of this case, which correctly lists both

of these Israeli priorities. Thus, the present application is in full compliance with the applicable regulation and there is no necessity to amend the declaration. Reconsideration and withdrawal of this objection is therefore respectful urged.

The examiner has objected to Figs. 11-15 for disclosing sequences that are not identified by a sequence identifier number. Further, the examiner states that Figs. 4-8 and 10 are objected to because each Y axis is not labeled.

With respect to SEQ ID NOs., the description of Figs. 11-15 in the specification has now been amended to insert SEQ ID NOs. As these sequences were already in the sequence listing of record, no amendment of the sequence listing is necessary. Accordingly, this part of the objection has now been obviated.

With respect to Figs. 4-8 and 10, new drawings are submitted herewith with proper labeling on the Y-axis. Thus, this objection has also been obviated.

The examiner states that the abstract has been objected to for having an unidentified abbreviation. While NIK is not an abbreviation, but is the official name for the protein, nevertheless, the abstract has now been amended to insert another name that is also acceptable for this protein, thus obviating this objection.

The examiner has objected to the specification for failing to recite the status of parent applications.

This objection is not understood as the first paragraph of the specification does not have any reference to

parent applications. Reference to parent applications in the first paragraph of the specification is not necessary when an application data sheet has been filed (see 37 CFR 1.78(a)(2)(iii)). As indicated above, an ADS is already of record in this case.

The examiner has also objected to the specification because the Table on page 57 is not numbered.

The specification has now been amended to insert the table number on page 57, and also to make all other corrections to the specification that have been noted during a review thereof. Accordingly, it is believed that this objection has now been obviated.

The examiner has objected to the claim set for not beginning with the sentence of which the claims are an object, e.g., "We claim" or "The claims are". This objection is respectfully traversed.

There is nothing in any statute or regulation, to the knowledge of the undersigned, that requires that these words actually appear in a patent application document. It is simply a fact that each claim is the object of a sentence that begins "We claim" or "The claims are." There is no necessity that these words actually appear anywhere. Furthermore, how would the examiner purpose that the claims be amended to insert this? Is it an amendment to the claims or an amendment to the specification? If an amendment to the claims, which claim is being amended? If it is an amendment to the specification, which page of the specification is being

amended? Reconsideration and withdrawal of this unnecessary formality is respectfully urged.

Claims 20, 23, 24, 66, 67, 69, 70 and 73-75 have been objected to for having an abbreviation "NIK" that is not defined.

While this is not an abbreviation, but the name of the compound, nevertheless, the other name of the compound has been inserted into the claims in order to clarify the claims for the examiner, thus obviating this objection.

Claims 74 and 75 have been objected to for reciting non-elected subject matter.

Claim 74 and 75 remain in the case as the full scope of these claims must be examined if a generic or linking claim is found to be allowable.

The examiner suggests improving the grammar of claim 20 by setting off the phrase "involving signaling of a cytokine through IL-2 cγc in the pathogenesis of said disease" by commas.

Claim 20 has now been amended to improve the grammar and to clarify the intended meaning thereof. The examiner's suggested improvement is not what was intended, as can be seen by the current language of the claim.

Claims 20, 23, 24, 66, 67, 69, 70 and 73-75 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The examiner states that the phrase "therapeutically effective" renders the claims indefinite as it is unclear what parameters of the disease are to be

analyzed and how effective the treatment must be in order to be "therapeutically effective." Similarly, the examiner states that the phrase "functional derivative" renders the claims indefinite as it is unclear what functions the derivative has. This rejection is respectfully traversed.

Claims 20, 66, 69, 70 and 73 have now been amended in order to clarify the terms "therapeutically effective" and "functional derivative." The term "therapeutically effective" has now been amended to read "an amount effective to bind to cγc and inhibit cγc/NIK interaction." This language is supported, for example, at page 19, lines 6-7, page 20, lines 9-10, page 21, lines 3-4, and page 23, lines 4-5. Similarly, with respect to the functional derivative, the function of all of the muteins, variants, fusion proteins, functional derivatives, circularly permutated derivatives and fragments has now been specified as maintaining the ability to bind to cγc and inhibit cγc/NIK interaction. Accordingly, both of these phrases have now been clarified and the claims are no longer indefinite.

The examiner states that the phrase "a host" renders the claims indefinite.

The claims have now been amended to change the term "a host" to read "a subject," as appears in the other claims. Accordingly, this part of the rejection has now been obviated.

Claims 20, 23, 24,, 66, 67, 69, 70 and 73-75 have been rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating allograft

rejection and adult T-cell leukemia using the polypeptide of SEQ ID NO:19, does not reasonably provide enablement for treating any disease involving signaling via any cγc using any variant of any NIK. The examiner states that the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of diseases to be treated with a large number of polypeptides. This rejection is respectfully traversed.

As discussed above, the present claims have now been amended such that their scope is now more directly related to the enabling disclosure. Thus, for example, with respect to claim 20, the claim specifies that the disease is one that involves signaling of a cytokine through cγc in the pathogenesis of the disease. The amount of NIK or related compound that is administered is an amount effective to bind to cγc and inhibits cγc/NIK interaction. Similarly, the related compounds are all defined as being ones that maintain the ability thereof to bind to cγc and inhibit cγc/NIK interaction. Accordingly, the claims no longer read on any variant, but only on those variants that maintain the ability of the NIK to bind to cγc and inhibit cγc/NIK interaction.

The specification explains how the inhibition of cγc/NIK interaction prevents effective signaling of the cytokine through the cγc of its receptor. Thus, those of ordinary skill in the art would expect that such a compound would indeed treat a disease that involves signaling of a cytokine through cγc. The same is true with respect to all of

the other independent claims. The claims no longer require testing an unlimited number of peptides. The terms used in the claims are defined in the specification. Accordingly, those of ordinary skill in the art would expect that the use of the defined compounds for treating the defined diseases would be operable and that it would not involve undue experimentation in order to practice the invention. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 20, 23, 24, 66, 67, 69, 70 and 73-75 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The examiner states that the claims are directed to a genus of methods for treating any disease involving signaling via any cγc using any variant of any NIK. While the specification teaches no such methods, the examiner states that the specification fails to describe any representative species of the genus by any identifying characteristics or properties other then the functionality of being a method for treating any disease involving signaling via any cγc using any variant of any NIK. Thus, the examiner considers that the specification fails to sufficiently describe the claimed invention. This rejection is respectfully traversed.

First of all, the examiner's terminology "via any IL-2 cγc" is not understood. There is only one cγc. It is the common gamma chain of a number of cytokines, such as IL-2, IL-12 and IL-15. However, every cγc is the same. To avoid

confusion, the term "IL-2" has now been deleted as the term "cγc" fully defines the chain that is being referred to in the claim.

As discussed above, the amendments to the claims now clarify that the claims correspond in scope to the disclosure. Representative species are indeed present in the specification, such as fragments of NIK represented by SEQ ID NO:19 and 18 and the mutant of NIK represented by AlyNIK. The *in vitro* tests in the present specification indicate the operability of such compounds in binding to cγc and inhibiting cγc/NIK interaction. The claims are now directed specifically to this function. Accordingly, one of ordinary skill in the art reading the present specification would understand that the present inventors were in possession of the invention as presently claimed. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 20 and 23 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Tinubu in view of Yamada and further in view of Luftig. Claims 20 and 23 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Waldmann in view of Yamada and further in view of Luftig. These rejections are respectfully traversed.

Yamada shows that NIK is involved in IL-2 production. However, Yamada does not teach the mechanism disclosed in the present specification involving cγc. Thus, it would not be obvious that the dominant negative NIK of Luftig would be able to treat cytokine dependent diseases for

all of the cytokines other than IL-2 that also have the cγc in their receptor. Accordingly, claim 20 has now been amended to add the proviso that the cytokine is other than IL-2. This claim is not made obvious by either Tinubu or Waldmann in view of Yamada and Luftig.

Furthermore, it is noted that the examiner has not included clam 24 in this rejection. New claim 76 is now, essentially, originally appearing claim 24 rewritten in independent form. Thus, this claim is patentable over the references of record for the same reason that the examiner indicated that claim 24 was free thereof.

Accordingly, reconsideration and withdrawal of this rejection is respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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